

2018-02-21

Integration of Patients into First-year Neuroscience Medical Curriculum

Follow this and additional works at: <https://hpe.researchcommons.org/journal>



Part of the [Health and Physical Education Commons](#)

Recommended Citation

(2018) "Integration of Patients into First-year Neuroscience Medical Curriculum," *Health Professions Education*: Vol. 4: Iss. 1, Article 9.

DOI: 10.1016/j.hpe.2017.02.001

Available at: <https://hpe.researchcommons.org/journal/vol4/iss1/9>

This Original Research Reports is brought to you for free and open access by Health Professions Education. It has been accepted for inclusion in Health Professions Education by an authorized editor of Health Professions Education.



Integration of Patients into First-year Neuroscience Medical Curriculum

Jasmine Pendergrass^a, Bianca Stewart^a, Kelsey Williams^a, James Buggy^a, Asa Black^a, Sandip Jain^b, Mary Hughes^b, Chris Troup^b, Thomas I. Nathaniel^{a,*}

^aUniversity of South Carolina School of Medicine, Greenville 29605, SC, USA

^bGreenville Health System, SC, USA

Received 19 November 2016; received in revised form 30 January 2017; accepted 3 February 2017

Available online 10 February 2017

Abstract

Background: A medical neuroscience curriculum that integrates broad categorization of neurological diseases in the first year of medical education has a functional utility to strengthen the foundation of medical students in clinical neuroscience. Students–patients interactive activities could provide an understanding of core curricula for basic neuroscience and clinical neurology.

Methods: Twelve neurological patients, with varying neurological diseases, volunteered to share their medical experiences with small groups of students in a 30-minute session. A debriefing segment with clinical and biomedical science faculty and students followed these sessions. Two structured student surveys – a pre and posttests were administered.

Results: 98.5% of students agreed (85.5% of these students strongly agreed) that patient integration into the first-year neuroscience module provided real-life experiences that were helpful in their understanding of clinical neuroscience. 95.6% of students agreed that their ability to interact with a diverse group of neurological patients was improved. Prior to the students–patients interactive session, only 91.1% of students agreed (52.6% of these students strongly agreed) that patient integration would be beneficial in their understanding of clinical neuroscience.

Discussion: The integration of patients into the neuroscience module provides better understanding of clinical concepts in neuroscience. It facilitates a meaningful discussions, stimulated critical thinking in neuroscience, and increased students' insights into patient–physician relationships, even at year one in the medical school, with significant real-life experiences.

© 2017 King Saud bin AbdulAziz University for Health Sciences. Production and Hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Neuroscience; Neurology; Medical education; Patients

1. Introduction

The recent integration of translational medicine in neurology into medical school curriculum, especially in

both the preclinical and clinical medical curriculum, brings more challenges in the development of session and program level objectives and assessment measures in medical school curriculum. To address this concern, the American Academy of Neurology (AAN) committee for undergraduate Education outlined a longitudinal competency-based curriculum in medical neuroscience that integrates clinical perspectives to preclinical coursework.¹ The committee developed core curricula that

*Corresponding author. Fax: +864 4558404.

E-mail address: nathanit@greenvillemed.sc.edu (T. I. Nathaniel).

Peer review under responsibility of AMEEMR: the Association for Medical Education in the Eastern Mediterranean Region

Table 1
Students interact with patients with different neurological disorders.

1. Temporal lobe epilepsy
2. Autoimmune epilepsy
3. Stroke with aphasia
4. Stroke s/p mechanical thrombectomy
5. Primary lateral sclerosis (ALS variant)
6. Myasthenia gravis
7. Charcot Marie Tooth,
8. Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIPD)
9. Multiple sclerosis
10. Multiple sclerosis
11. Parkinson's disease
Migraine headaches, post-concussion syndrome via traumatic brain injury

integrates basic neuroscience with clinical neurology, and highlighted specific learning objectives for each of the 6 competencies (Medical knowledge, Patient care, Interpersonal and Communication skills, Professionalism, Practice Based learning, and Systems Based Practice) to connect the normal neuroanatomy, neurophysiology, neuroembryology or biochemical functions with abnormal correlations.

Several new and old medical schools are now restructuring their curricula in line with the 6 core competencies. Despite this new development, there is a general variation in Neuroscience curriculum among medical schools in the United States.^{2,3} This is because some medical schools teach basic neuroanatomy, neuroembryo, neurohistology or neurophysiology in year 1 and abnormal correlations such as neuropathology, pathophysiology, and pharmacology in mind brain and behavior – a year 2 course.^{4–9} Other medical schools actually teach neuroscience topics in one combined preclinical course outside the neuroscience-designated coursework whereas, others still teach the basic sciences as independent disciplines without integration into a systems-based approach. Since neurologic diseases account for approximately 7% of outpatient office and over 5% of emergency room visits,^{10–12} the next generation of neurologist-scientists needs a strong basic neuroscience medical education to be able to advance the understanding of the fundamental pathophysiologic underpinnings of nervous system disorders. The Neuroscience curriculum in the University of South Carolina School of Medicine Greenville (USCOMG) is broad and structured with an integrated preclinical/clinical model, with a functional utility in medical education within diverse biomedical science courses. This approach integrates the basic normal functioning of the nervous with

clinical neurology to provide a core neuroscience curriculum with a strong foundation in clinical neuroscience and medical education.^{12–17} A major component of the USCOMG neuroscience module is the integration of patients with different neurological disorders into a year 1 neuroscience module. We describe the integration of student–patient interactions into a year one neuroscience medical curriculum to integrate basic neuroscience and neurology into year one core curriculum to provide students the additional exposure to neurology and neuroscience.

2. Methods

2.1. Organization of the neuroscience module

Neuroscience is a four week module that integrates the development, anatomy, biochemistry and physiology of the central and peripheral nervous system with clinical correlates. The principles that underlie the anatomical structures of each system are correlated with their physiology and relevant clinical applications. Students are expected to learn how to integrate the normal molecular, cellular, physiological, and anatomical aspects of the nervous system in order to understand the basis of disorders commonly encountered in clinical practice. Weekly topics are structured into themes that include an anatomical and functional organization of the nervous system (week 1), morphological and functional correlates of neuronal activity (week 2). Week 3 focuses on vascular supply of the nervous system, while motor and sensory systems were the focus of week. The students–patients interactive session is a 3 h session of activities in week 3 of the neuroscience module.

2.2. Patient selection criteria

Neurological patients of the Greenville Memorial Health System (GMH) volunteered to share their personal life experiences in various neurological conditions. The different neurological conditions are presented in Table 1. Each patient interacted with a small group of 10–12 first-year medical students. The focus on neurology patients is to provide clinical experiential learning to facilitate students' basic understanding of neurological disorders, and patient experience. Moreover, this will enhance the correlation between concepts and disease processes learned in class and clinical presentations. Fig. 1 presents the schematic representation of the experimental design used in the present study.

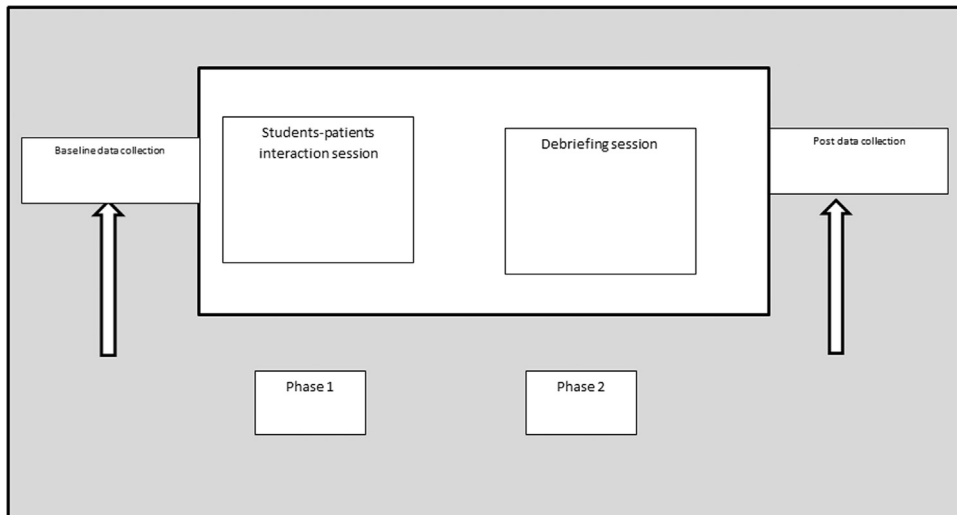


Fig. 1. Schematic representation of the experimental design used in the present study. Data on students' expectations were collected prior to the student-patient interaction sessions to generate a baseline. Post-test evaluation was carried out after the debriefing session to evaluate students' perception of the students–patients interactive session.

2.3. Grouping of students and patients during the interactive session

Students were randomly divided into small groups of 10–12 individuals. Each group was paired with a patient and allotted 30 min. After the first session, each group transitioned to a different small group room in order to interact with a second patient for another 30 min, such that each student interacted with at least two patients with Neurological conditions for one hour. In order to maximize the student-patient learning experience, faculty and clinicians were not present during these sessions. During the interactive session, patients shared their experiences with students in an informal open discussion, and students also had the opportunity to ask questions. In this context, year one students now have contact with patients during their pre-clinical medical education. This pre-clinical familiarization of medical students with patients improves students' understanding of patients' perceptions, helps students understand patients as human beings, and helps them recognize the importance of the doctor–patient relationship unity to discuss the pathophysiological basis of their clinical conditions, symptoms, and treatment.

2.4. Debriefing and general discussion session

After the interaction with patients, students met collectively in a large lecture hall with a sitting capacity of 150 students to participate in a debriefing session

with clinical faculty and neurologists involved in the patients' care. The debriefing session provided the opportunity for each group to share the patient interaction experience with their colleagues who did not have the opportunity to interact with the patient in their small group session. Patients were not present during the debriefing session, and this preserved their privacy and maximized the educational exchange between biomedical science faculty, neurologists and students. Specifically, each group had the opportunity to provide an oral summary of the patient they interacted with to the class as a whole. The groups' summaries were supplemented with clinical knowledge from biomedical science faculty and physicians. While students were unable to meet with all of the patients, the panel discussion provided a significant amount of information about patient experiences and clinical conditions for the class to learn. In general, the panel discussion allowed for the entire class to learn a significant amount of information about the clinical conditions and experiences of patients they had not spent personal time with.

2.5. Data collection

Multiple-choice questionnaires were designed on medical student responses to students–patients interactive pre-and post-test sessions. The questionnaire includes seven items on medical students' expectations prior and post implementation of the interactive, student-patient educational session called “Meet the

Table 2

Presents students expectations prior (pretest) to the implementation of student–patient educational interactive session and the posttest evaluation.

	Pretest evaluation					Posttest evaluation					P-value
	Strongly disagree	Disagree	Neutral	Agree	Strongly agree	Strongly disagree	Disagree	Neutral	Agree	Strongly agree	
The session improves my ability to better integrate my basic neuroscience and understand neurological issues.	0	0	8.8%	57.9%	33.3%	0	0	4.3%	30.4%	65.2%	0.0057*
The session provides meaningful discussion and learning to stimulate critical thinking in neuroscience	0	0	7.01%	50.9%	42.1%	0	0	0	20.3%	79.7%	0.0003*
This provides real-life experiences that will be beneficial in my future and continuous clinical training	0	0	8.8%	38.5%	52.6%	0	0	1.4%	13.0%	85.5%	0.0012*
The session provides a productive time and helpful in highlighting how neurological problems affect the patients' lives	0	0	7.01%	29.8%	63.2%	0	1.4%	1.4%	13.0%	84.1%	0.0123*
This session provides insight on patients' encounters with physician, that will helpful in relating to patients in the future.	0	1.8%	5.3%	42.1%	50.1%	0	0	2.9%	18.8%	78.2%	0.0126*
I expect this session to meet and/or exceed my learning expectations	0	1.8%	29.8%	43.9%	24.6%	0	0	1.4%	26.1%	72.5%	.0.0001*
This session will help in understanding how patient experiences can be different and/or similar to clinical concepts learned in the class	0	0	5.3%	49.1%	45.6%	0	0	1.4%	17.4%	81.2%	0.0038*

Patients". A 5-pt Likert scale with a score of 1=Strongly Disagree, 2=Disagree, 3=Neutral, 4=Agree, and 5=Strongly agree was used to gather student feedback regarding the sessions. The surveys were anonymous and included a section for additional comments to allow for student feedback on strengths, weaknesses, and suggestions for future students–patients interactive session.

2.6. Data analysis

Students' expectations (pretest) prior to the implementation of students–patients interactive sessions and satisfaction of students with the students–patients interactive session (post-test) were expressed in percentages and presented in Table 1. A contingency analysis for the frequency distribution of the variables was used to provide a basic picture of the interrelation between the pre and posttest variables, and to help determine interactions between them. The significance of the difference between the pre and posttests was determined using the Pearson's chi-squared test. Differences in proportions and *P*-values with 95% confidence intervals were considered significant. All analyses were descriptive – involving means, percentages, and other descriptive statistics. All statistical analyses were performed using SAS Statistical Software (Cary, North Carolina).

3. Results

Table 2 presents students' expectations prior (pretest) to the implementation of students–patients educational interactive session and the posttest evaluation. Over 90% of students either agreed or strongly agree and expect that the students–patients interactive activity will improve their ability to better connect their understanding of basic neuroscience with neurological issues, gain additional exposure to neurology and neuroscience beyond the school's curriculum, promote meaningful discussions and learning opportunities to stimulate critical thinking in neuroscience. Majority of the students (91.2%) expect that the session will provide increased insight into the patients' quality of life and patient–physician relationships even at year one of their medical school career, and provide real-life experiences that will be beneficial in their future and continuous clinical training. Between 7.01% and 8.8% of students were neutral or disagreed with the above possible benefits of the students–patients interactive session in the neuroscience module. 94.7% of students either agreed or strongly agreed with the expectation

that integrating neurological patients into the neuroscience module will contribute to their understanding of clinical concepts learned in a classroom setting, while 5.3% of students were neutral. 92.2% of the students expect the session to provide an insight into patients' encounters with physician, that will be helpful in relating to patients in the future. Overall, 68.5% of students either agreed or strongly agreed that the students–patients interactive sessions would meet or surpass their expectations while 31.6% remained neutral or disagreed.

For the posttest evaluation, over 95% of students either agreed or strongly agreed that the student–patient interactive session significantly ($P < 0.001$) improved their ability to better integrate their understanding of basic neuroscience with neurological issues, and allowed them to gain additional exposure to neurology and neuroscience beyond the school's curriculum. The students–patients interactive session significantly ($P < 0.001$) promoted meaningful discussions, learning opportunities, stimulated critical thinking in neuroscience, and increased students insights into patient–physician relationships and provided real-life experiences.

Between 1.4% and 4.3% of students were neutral or disagreed with the above benefits of the sessions, while 98.6% of students either agreed or strongly agreed that integrating patients into a neuroscience curriculum improved their understanding of clinical concepts learned in a classroom setting. About 1.4% of students remained neutral. The overwhelming majority of students (98.6%), either agreed or strongly agreed that the students–patients interactive sessions met or surpassed their initial expectations while 1.4% remained neutral. Overall, 59.4% the students strongly agreed, 31.8% agreed with the organization of the session, while 4.3% were both neutral and disagrees respectively. 82.6% of the students strongly favored the intimate small group setting over a larger, panel-style discussion, while 11.6% agree and 5.8% of the students were neutral, and no students disagree or strongly disagree with students–patients interactive small group setting. Finally, 98.6% of students recommended similar sessions for future neuroscience classes.

4. Discussion

Although at present, the LCME does not mandate medical schools to provide a formal structured neurology program during the preclinical and clerkship years, it is advisable for schools to have their students have clinical encounters with neurologic patients to reflect

upon their clinical experiences and medical training.^{4,18–20} This encounter is important as most of the neuroscience and neurology contents of many medical school's curriculum appear to be taught outside the neuroscience-designated coursework. For instance, neurological diseases such as sleep apnea, Myasthenia Gravis, or myotonic dystrophy are often discussed in a cross-disciplinary context in pulmonary, endocrinology, and genetics. Moreover, basic cellular and molecular concepts of neurologic diseases are often learned in biomedical science coursework outside of neuroscience.^{4,21–23} Therefore, a medical neuroscience curriculum that integrates broad categorization of neurological diseases in the first year of medical education has a functional utility to strengthen the foundation of medical students in clinical neuroscience.^{7,24–26}

Our findings show that providing first-year medical students with the early interactive experiences with actual patients helps to personalize real-life scenarios and strengthen the clinical concepts learned in the classroom setting. This is important to advance students understanding of the fundamental broad categories of nervous system disorders with the experiential experience of interacting with patients.^{27–35} In this context, our students not only gained a better understanding of neurological problems, but also gleaned knowledge surrounding the family challenges faced by these neurological conditions. Students reported that the students–patients interactive session improved their ability to interact with a diverse group of patients. Such opportunities are undeniably important to fostering a broader set of skills and attitudes, which will allow year one medical students to effectively grow throughout their medical training as they transition into the clerkship years.^{36–39} In addition, the integrated teaching of clinical and basic biomedical science aspects of neuroscience also improves learning and is a major strength of our curriculum.

Our study was limited in that it was a new implementation into the curriculum that will require future improvements to provide the most beneficial experience for students. Thus, while we were able to recruit twelve patients for the session, only ten patients actually participated. This caused two student groups to be dispersed, making some groups larger than intended, subsequently, contributing to organizational issues. Also, time constraints posed limitations as well. While we felt each patient provided diversity in regards to their array of conditions, scheduling only allotted students to directly interact with two patients. In the future, we hope to create a series of students–patients

interactive sessions that create the opportunity for students to interact with a larger portion of the patient volunteers. Per survey comments, several students suggested weekly students–patients interactive sessions throughout our 4-week module.

5. Conclusion

In this study, we demonstrated that real-life patient encounters, followed by relevant clinical discussion helps to enhance the understanding and learning of clinical concepts for first-year medical students.

One sentence bios

Jasmine Pendergrass is a year two medical student at the University of South Carolina School of Medicine-Greenville, SC, USA.

Bianca Stewart is a year three medical student at the University of South Carolina School of Medicine-Greenville, SC, USA.

Kelsey Williams is a year two medical student at the University of South Carolina School of Medicine-Greenville, SC, USA.

Dr James Buggy is a Neuroscientist and the Associate Dean for Students Affairs at the University of South Carolina School of Medicine-Greenville, SC, USA.

Dr Asa Black is a Professor of Anatomy and Neuroanatomy at the University of South Carolina School of Medicine-Greenville, SC, USA.

Dr Sandip Jain is a Neurologist at the Greenville Health System, SC, USA.

Dr Mary Hughes is a Neurologist at the Greenville Health System, SC, USA.

Dr Chris Troup is a pediatric Neurosurgeon at the at the Greenville Health System, SC, USA.

Dr Thomas I Nathaniel is a Neuroscientist and the Director for the Neuroscience Module at the University of South Carolina School of Medicine-Greenville, SC, USA.

Disclosure

Ethical approval. Ethical approval has been granted for this study.

Other disclosure

None.

Acknowledgements

We thank Year one Medical Students of the University of South Carolina School of Medicine Greenville for participating in the data collection. We thank Dr. Melinda Ingjaimo for editing the initial version of the manuscript.

References

1. Scoles PV. Comprehensive review of the USMLE. *Adv Physiol Educ* 2008;32(2):109–110.
2. Holden KR, Cooper SL, Wong JG. Neuroscience curriculum changes and outcomes Medical University of South Carolina, 2006 to 2010. *Neurologist* 2012;18(4):190–195.
3. Shapiro J. The paradox of teaching empathy in medical education. *Empathy: Bench Bedside* 2012:275–290.
4. Merlin LR, Horak HA, Milligan TA, Kraakevik JA, Ali II. A competency-based longitudinal core curriculum in medical neuroscience. *Neurology* 2014;83(5):456–462.
5. Billings-Gagliardi S, Fontneau NM, Wolf MK, Barrett SV, Hademenos G, Mazor KM. Educating the next generation of physicians about stroke – incorporating stroke prevention into the medical school curriculum. *Stroke* 2001;32(12):2854–2858.
6. Cunningham JT, Freeman RH, Hosokawa MC. Integration of neuroscience and endocrinology in hybrid PBL curriculum. *Adv Physiol Educ* 2001;25(4):233–240.
7. Giffin BF, Drake RL. Gross anatomy of the head and neck and neuroscience in an integrated first-year medical school curriculum. *Anat Rec* 2000;261(2):89–93.
8. A.R. Pearce, K. Biondolillo, M. Srivatsan. Enhancing faculty student experiences neuroscience a predominantly undergraduate institution. 2010.
9. Sanya EO, Ayodele OE, Olanrewaju TO. Interest in neurology during medical clerkship in three Nigerian medical schools. *BMC Med Educ* 2010;10.
10. Hootman JM, Helmick CG, Schappert SM. Characteristics of ambulatory medical care visits among persons with arthritis and other rheumatic conditions. United States, 1997. *Arthritis Rheum* 2000;43(9):S138.
11. Stettler BA, Jauch EC, Kissela B, Lindsell CJ. Neurologic education in emergency medicine training programs. *Acad Emerg Med* 2005;12(9):909–911.
12. Schappert SM, Burt CW. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 2001–02. *Vital Health Stat* 2006;13:1–66.
13. Whitcomb ME. The teaching of basic sciences in medical school. *Acad Med* 2006;81:413–414.
14. Hudson JN. Linking neuroscience theory to practice to help overcome student fear of neurology. *Med Teach* 2006;28(7):651–653.
15. Miller L, Schweingruber H, Oliver R, Mayes J, Smith D. Teaching neuroscience through web adventures: adolescents reconstruct the history and science of opioids. *Neuroscientist* 2002;8(1):16–21.
16. Resnick DK. Neuroscience education of undergraduate medical students. Part I: role of neurosurgeons as educators. *J Neurosurg* 2000;92(4):637–641.
17. Resnick DK, Ramirez LF. Neuroscience education of undergraduate medical students. Part II: outcome improvement. *J Neurosurg* 2000;92(4):642–645.
18. Esteves JE, Spence C. Developing competence in diagnostic palpation: perspectives from neuroscience and education. *Int J Osteopath Med* 2014;17(1):52–60.
19. Gould DJ, Clarkson MJ, Hutchins B, Lambert HW. How Neuroscience is taught to North American dental students: results of the basic science survey series. *J Dent Educ* 2014;78(3):437–444.
20. Hall S, Stephens J, Andrade T, Davids J, Powell M, Border S. Perceptions of junior doctors and undergraduate medical students as anatomy teachers: investigating distance along the near-peer teaching spectrum. *Anat Sci Educ* 2014;7(3):242–247.
21. Abdullah JM. Another important news from the neuronman: malaysia's neuroscience group moves upwards in terms of research, creativity, and innovation. *Malays J Med Sci* 2015;22:1–4.
22. Albert DV, Yin H, Amidei C, Dixit KS, Brorson JR, Lukas RV. Structure of neuroscience clerkships in medical schools and matching in neuromedicine. *Neurology* 2015;85(2):172–176.
23. Anandkumar S. Effect of pain neuroscience education and dry needling on chronic elbow pain as a result of cyberchondria: a case report. *Physiother Theory Pract* 2015;31(3):207–213.
24. Charles PD, Scherokman B, Jozefowicz RF. How much neurology should a medical student learn? A position statement of the AAN undergraduate education subcommittee. *Acad Med* 1999;74(1):23–26.
25. Griffin JD. Technology in the teaching of neuroscience: enhanced student learning. *Adv Physiol Educ* 2003;27(3):146–155.
26. Swanson JW, Hammack JE, Benarroch EE. Teaching neuroscience and clinical neurology in an integrated curriculum for medical students. *Neurology* 1999;52(6):A66.
27. Stettler BA, Jauch EC, Kissela B, Lindsell CJ. Neurologic education in emergency medicine training programs. *Acad Emerg Med* 2005;12.
28. Gelb DJ, Gunderson CH, Henry KA, Kirshner HS, Jozefowicz RF, Consortium Neurology Clerkship D.. The neurology clerkship core curriculum. *Neurology* 2002;58(6):849–852.
29. Bermejo-Pareja F, Hernandez-Gallego J. What should a medical student know about neurology? A review. *Rev De Neurol* 2007;44(6):360–365.
30. Cockerell OC, Goodridge DMG, Brodie D, Sander J, Shorvon SD. Neurological disease in a defined population: the results of a pilot study in two general practices. *Neuroepidemiology* 1996;15(2):73–82.
31. Davis LE, King MK. Evaluating medical students' performance in a clinical setting. *Nat Clin Pract Neurol* 2007;3(12):702–703.
32. Gelb DJ. Where's the logic in neurologic education?. *Exp Neurol* 2003;184:S48–S52.
33. Anwar K, Shaikh AA, Sajid MR, Cahusac P, Alarifi NA, Al Shedoukhy A. Tackling student neurophobia in neurosciences block with team-based learning. *Med Educ Online* 2015;20.
34. Flannery T, Gormley G. Evaluation of the contribution of theatre attendance to medical undergraduate neuroscience teaching – a pilot study. *Br J Neurosurg* 2014;28(5):680–684.
35. Lukas RV, Cooper B, Morgan I, Brorson JR, Dong HM, Sherer R. Attitudes toward neurosciences in medical students in Wuhan, China: a survey study. *World Neurosurg* 2014;82(3–4):266–269.

36. Minhas P, Chu YX, Mata DA. Neuropathology: bridging psychiatry and neurology in medical education. *Lancet Psychiatry* 2016;3(2):98–100.
37. Popeo DM, Goldstein MA. Design and piloting of an integrated neuroscience elective for medical students in their clinical clerkships. *Acad Psychiatry* 2016;40(2):359–362.
38. Preusche I, Lamm C. Reflections on empathy in medical education: what can we learn from social neurosciences?. *Adv Health Sci Educ* 2016;21(1):235–249.
39. Schildkrout B, Benjamin S, Lauterbach MD. Integrating neuroscience knowledge and neuropsychiatric skills into psychiatry: the way forward. *Acad Med* 2016;91(5):650–656.